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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/541,848	04/03/2000	Jiandong Chen	98,057-G	4238

7590 04/18/2002
David W. Clough
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EXAMINER

WANG, ANDREW J

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 04 18, 2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/541,848

Applicant(s)

CHEN ET AL.

Examiner

Andrew Wang

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-29 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Response to Arguments

1. Claims 1-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-43 of copending Application No. 09/383,507 for the same reasons of record as set forth in the Office action mailed 13 August 2001.

Applicants have requested to hold the rejection in obedience until allowable subject matter is indicated. No further arguments have been provided in the response filed 6 February 2002.

2. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/20238 for the same reasons of record as set forth in the Office action mailed 13 August 2001.

Applicants' arguments filed 6 February 2002 have been fully considered but they are not persuasive. Applicants argue that although '238 teaches that MDM2 can be inhibited by antisense oligos, the reference does not teach the increase in p53 expression. Although the increase in p53 expression was not explicitly taught by '238, the reference does teach the same method steps as claimed by applicants and thus anticipate applicants claimed invention since the increase in p53 expression would be inherent the method steps of '238.

3. Claims 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Kondo et al. for the same reasons of record as set forth in the Office action mailed 13 August 2001.

Applicant's arguments filed 6 February 2002 have been fully considered but they are not persuasive. Applicants argue that Kondo would not anticipate the claimed invention since Kondo teaches that the administration of MDM2 sense and antisense oligos did not increase the expression of p53 in cisplatin treated cells. Although MDM2 antisense oligos did not increase the expression of p53 in cisplatin treated cells, it does not preclude said antisense oligos increasing p53 expression in untreated cells. It is presumed that the cisplatin treatment maximally induced p53 expression thus preventing further p53 expression by antisense treatment.

4. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kondo et al. in view of Clark et al. for the same reasons of record as set forth in the Office action mailed 13 August 2001.

Applicant's arguments filed 6 February 2002 have been fully considered but they are not persuasive. Applicants provide essentially the same arguments that have been addressed above.

5. Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification is only enabling for a method of inhibiting tumor cells, in vitro, using MDM2 antisense oligos and a method of inhibiting tumor cells in vitro or in vivo using SEQ ID

NO: 28 or 47. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for the same reasons of record as set forth in the Office action mailed 13 August 2001.

Applicant's arguments filed 6 February 2002 have been fully considered but they are not persuasive. Applicants argue that Agrawal teaches several studies that show the effectiveness of antisense therapy in a variety of circumstances but contrary to applicants assertions of in vivo efficacy in treatment, Agrawal does not teach successful treatment of any disease or ailment. Agrawal merely points out some successes with in vivo delivery without citing any actual treatments.

Furthermore, applicants assert that the artificial systems as described by Agrawal are limited to those assay systems that use transfected or partial gene sequences not normally expressed is noted but Agrawal further infers that it is unclear as to whether cell culture or animal models are appropriate for studying antisense oligos (page 384). As can be seen, the activity of any particular antisense oligo is unpredictable since the appropriate study model is not readily available. Moreover, applicants assertion that since the specification shows the efficacy of SEQ ID NO: 28 and 47, in vivo, applicants have enabled the breadth of the claimed invention. Although it is agreed that applicants have enabled the in vivo use of SEQ ID NO: 28 and 47, applicants have not enabled the breadth of the claimed invention that is drawn to any antisense oligo in vivo. As applicants note, Agrawal on page 385, teaches that animal models may be necessary for confirming antisense activity after tissue culture screening. Applicants have only

tested SEQ ID NO: 28 and 47 in animals, which is not considered representative of the genus sought.

Additionally, applicants cite the standards in the art for publishing articles claiming antisense inhibition and that applicants have complied with the standards but the rejection of record is drawn specifically to in vivo inhibition and its unpredictability not in vitro inhibition. In fact, the rejection of record does not question applicants in vitro methods and clearly states that the in vitro antisense inhibition methods are enabled. Moreover, applicants disclosure of the in vitro activity of specific oligos do not remedy the unpredictability of antisense treatment in vivo since the cited art clearly teaches that antisense oligo effects must be considered on a "case-by-case-basis" (Branch).

Lastly, applicants assert that the *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 U.S.P.Q.2d 1129 decision is applicable in the instant rejection but contrary to applicants assertions the Enzo decision was based on the antisense compositions, not in vivo methods. Although it is accurate that the Enzo decision addresses enablement of antisense compositions, said decision is not applicable in the instant rejection since the rejection states that applicants are enabled for the antisense compositions and its in vitro use. Applicants specification including the specific examples do not remedy the unpredictability of antisense treatment since applicants have only shown two oligos with any type of in vivo efficacy. Said disclosure is not sufficient to enable the claimed genus since each oligo needs to be tested empirically as supported by Branch who states that "internal structures of target RNAs and their associations with cellular proteins create

physical barriers, which render most potential binding sites inaccessible to antisense molecules" (page 45, third column).

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

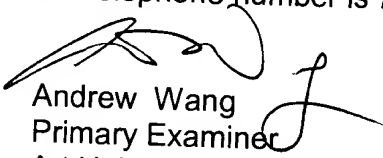
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew Wang whose telephone number is 703-306-3217. The examiner can normally be reached on Monday thru Thursday, 6:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

AJW
April 10, 2002



Andrew Wang
Primary Examiner
Art Unit 1635